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The Mercury Connection: Autism and Childhood Vaccines

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Thesis: Thimerosal may be a contributing factor of Autism, requiring more research.

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"Giving a ten-pound infant a single vaccine in a day is the equivalent of giving a 100 pound adult 40 vaccines in a day… we are not talking about causing death; we are talking about causing Autism. As a scientist, you have to ask yourself, what's the most obvious neurotoxin that these children are being exposed to that could cause this? Thimerosal." (Morrison, 2002).[1]

Thimerosal, a mercury-containing organic compound has been used as a preservative in the United States since the 1930s in many biological and drug products, including many vaccines to help kill or prevent the growth of harmful microorganisms (Food and Drug Administration, 2008). Since 2004 all vaccinations recommended for children 6 years and younger contain no Thimerosal. Despite the fact that the Food and Drug Administration (FDA) along with other federal health organizations, such as the Center for Disease and Controls Preventions (CDC) maintain that there is no connection between Thimerosal and Autism, a nuerodevelopmental disorder, the concern remains. The correlation, between an increasing number of Thimerosal containing vaccines on the infant immunization schedule and the dramatic rise in diagnosis of Autism suggests that Thimerosal may be a contributing factor of Autism. The

[1] Quote from Dr. Boyd Haley, Chair of the University of Kentucky Chemistry Department, 2003 House of Representatives testimony on the effects of Thimerosal.

reliance on flawed, outdated, or discounted studies requires that more research be conducted.

Mercury has been described by the National Autism Association, and in a House Congressional Report on Mercury in Medicine as "hazardous to humans"; however, the U.S. Federal Food and Drug Administration (FDA) emphasizes that there are significant distinctions between organic and inorganic forms of mercury. Furthermore, FDA literature stresses a distinction between the two forms of mercury. That is, methyl-mercury, the organic form of mercury, is a neurotoxin, while ethyl-mercury, an inorganic form of mercury (of which Thimerosal is a compound) has the "theoretical potential" for neurotoxicity (Autism Society of Boulder County, 2008; FDA, 2008).

During the late 1950s and 1960s the toxicity of methyl-mercury was first recognized for the accidental discharge of mercury in Minimata Bay, Japan, that led to widespread consumption of mercury-contaminated fish (FDA, 2008). Also in the 1970s, an additional incident of methyl-mercury poisoning occurred in Iraq when grain was treated with methyl-mercury and then used to make bread (FDA, 2008). In both the Japan and Iraq incidences, maternal exposures to high levels of the methyl-mercury led to infants exhibiting severe neurological injury, including a

condition resembling that of cerebral palsy and also motor, sensory and developmental delays (FDA, 2008). As a result of these accidental exposures to toxic levels of methyl-mercury, several national and world organizations developed guidelines for 'safe' exposure levels for methyl-mercury. These exposure levels range from 0.1 micrograms of methyl-mercury/kg of body weight/day (Environmental Protection Agency) to 0.47 micrograms of methyl-mercury/kg of body weight/day (World Health Organization), the range of which varies based on each agencies varying safety margin and the population based on which each agency serves (FDA, 2008).

In regards to ethyl-mercury, the FDA maintains that there is a lack of comparative definite data on the toxicities of ethyl and methyl-mercury, and therefore the FDA "considers ethyl- and methyl-mercury as equivalent" (FDA, 2008). Furthermore, the FDA along with other federal agencies have determined that in the absence of a specific standard for ethyl-mercury, the limits for ingested methyl-mercury should be used for injected ethyl-mercury (FDA, 2008).

While absence of data on ethyl-mercury necessitated the use of safety guidelines that were originally developed for methyl-mercury, a recent study comparing the blood and brain mercury levels in infant monkeys exposed to methyl-

mercury and ethyl-mercury found that methyl-mercury is in fact not a suitable reference for extrapolating information about ethyl-mercury (Burbacher et. al, 2005).

Despite conflicting studies, the FDA maintains that, as an ethyl-mercury compound, not only is Thimerosal an effective vaccine preservative but also that it is a safe level in terms of exposure. One study referenced by the FDA, Powell and Jamieson (1931) administered a 1% Thimerosal solution to twenty-two individuals "for unspecified therapeutic reasons," with the majority of subjects experiencing no reported toxic effects (FDA, 2008). Also the FDA noted that Cox and Forsyth (1988) and Grabenstein (1996) found only allergic responses to Thimerosal, for "no ill effects other than minor local reactions at the site of injection" (FDA, 2008).

As noted in the studies referenced by the FDA, findings suggest that since Thimerosal's inception, Thimerosal has always been regarded as a relatively safe product. Kennedy (2005) states, however, that internal documents from Eli Lily, which first developed Thimerosal, show that Lily knew from the product's inception that Thimerosal could cause harm and even death. According to Kennedy (2005) in 1930, Eli Lily tested Thimerosal by administering it to twenty-two individuals with terminal

meningitis, all of whom died within weeks of being injected, thus suggesting the harm of Thimerosal. Kennedy (2005) also states that in 1935 researchers at another vaccine manufacturer, Pittman-Moore, warned Eli Lilly that its claims about Thimerosal's safety did not concur with Pittman-Moore's findings. Furthermore, half the dogs Pittman had injected with a Thimerosal-based vaccine became sick, leading researchers to declare Thimerosal "unsatisfactory as a serum intended for use on dogs" (Kennedy, 2005).

Concern about the levels of ethyl-mercury to which children were being exposed increased during the mid-1990s. During that period the number of Thimerosal-based vaccines American children were receiving increased dramatically (Kennedy, 2005). Prior to 1989, American children received only three vaccines: Polio, Diphtheria-Tetanus-Pertussi (DTaP) and measles-mumps-rubella (MMR)(Kennedy, 2005). Approvals in the early 1990s by the Advisory Committee on Immunizations Practices (ACIP) resulted in an increase in children's vaccines, thus raising the number of immunizations to twenty-two by the time children were in first grade (Geier & Grier, 2003; Kennedy, 2005). With this increased number of immunizations, by six months children already had "unprecedented levels of mercury during a

period critical for brain development," and had been injected with levels of ethyl-mercury eighteen times greater than the EPA's limit for daily exposure to methyl-mercury (Kennedy, 2005).

Over the same period, in which there was an increase in the number of Thimerosal-containing vaccines children were receiving, there was also a dramatic rise in the rate of Autism in American children. While the Center for Disease and Control Protections (CDC) did not start to monitor Autism rates until 1996, the American Medical Association reports a low rate of Autism for the 1980s, of 4 per 10,000 children (Yeargin-Allsopp, M. et al, 2003). In comparison to the rate of Autism in the 1980s, during the late 1990s Autism increased dramatically, for in 1996 the CDC reported the rate of Autism as 4.2 per 1,000 children, a rate which increased to 6.7 per 1,000 children in 1998 and 2000 (CDC, 2008).

As the 1990s saw an increase in ethyl-mercury containing vaccinations and a rise in Autism, concern grew about the link between the variables. To address growing public concern, in 1997, the FDA Modernization Act began a comprehensive review of all mercury containing food and drug products. In 2001, the Institute of Medicine (IOM) Immunization Safety Review Committee issued a report on the

review, concluding that evidence was inadequate, and a causal relationship between Thimerosal-containing vaccines and Autism could not be rejected or accepted (FDA, 2008). However, a second and final report was issued in 2004, which rejected a possible causal relationship between Thimerosal-containing vaccines and Autism (FDA, 2008).

Although their 2004 report found no link between Thimerosal-containing vaccines and Autism, controversy at a 2001 IOM meeting on Thimerosal-Containing Vaccines and Neurodevelopmental Outcomes, offers substantial support to a relationship between Thimerosal-containing vaccines and Autism. During a July 2001 IOM meeting, findings were presented from the CDC's Thimerosal Vaccine Safety Data-Link Study (VSD), which evaluated nuerodevelopmental injury and exposure to Thimerosal, at one and three months of age by studying the health records of over 100,000 children at four HMOs (Morrison, 2002). At the IOM meeting it was presented that there was a 1.69 relative risk of Autism connected to Thimerosal exposure. However, a 2000 confidential version of the VSD study (obtained through the Freedom of Information Act), as well as transcripts from a scientific review of this confidential version (which took place at Simpsonwood Retreat Center) placed the relative risk significantly higher, at 2.48 (Morrison, 2002). The

increased risk connected to Thimerosal exposure was echoed by several of the scientists present at the Simpsonwood Retreat, with one at the conference stating: "an exposure to more than 62.5 micrograms of mercury within the first three months of life significantly increases a child's risk of developing nuerodevelopmental orders such as speech and language delay, autism, stuttering, and attention deficit disorder" (Morrison, 2002).

While the same dataset was used in both versions of the VSD study, the 2001 version presented at the IOM meeting had an additional 34,334 children. According to both Morrison (2002) and SAFEMINDS (2008) children where added to the study and thus affected the relative risk associated with Thimerosal when the inclusion criteria for the study was altered. Further, according to Morrison (2002) and SAFEMINDS, (2008) the original HMO data cycle used in the study was updated and an additional year, 1998, was added, yielding the relative risk that was presented at the IOM meeting. Furthermore, Morrison (2002) and SAFEMINDS (2008) claim that the children added to the study would have been too young to have been diagnosed with Autism, for at the time the study occurred the children would have just been turning two, and Autism on average is diagnosed after 44 months (Morrison, 2002).

Following the IOM's 2004 rejection of the relationship between Thimerosal- Autism, many government and non-government studies concurred with IOM's findings. However, in an independent study, Geier and Geier (2006) refuted the IOM's position, finding a connection between neurodevelopment disorders and Thimerosal in childhood vaccines. The use of the CDC's Vaccine Adverse Event Reporting System (VAERS) database and the California Department of Developmental Services (CDDS) Early Downward Trends in Neurodevelopmental Disorders Following Removal of Thimerosal-Containing Vaccines, the Geier and Geier (2006) study provided "strong epidemiological evidence for a link between increasing mercury from Thimerosal-containing childhood vaccines and neurodevelopmental disorders" (Geier and Geier 2006).

Further support of the Autism-Thimerosal connection can be found looking at the rates of Autism in countries that have already removed Thimerosal or similar mercury based preservatives from their children's vaccines. While Thimerosal is no longer used as a preservative in U.S. vaccines routinely recommended for children six years and younger (with the exception of inactivated influenza vaccine), the removal of Thimerosal only took place in 2004 (FDA, 2008).

In comparison, Denmark removed all mercury preservatives from vaccinations in 1992. Prior to the removal of mercury preservatives, Danish Autism rates were 0.2 per 10,000; however, following the removal of mercury preservatives from vaccines, the Autism rate rose 2-5 per 10,000 by 2000, a fact that has led many studies to disregard the impact of removing mercury preservatives from vaccines. According to both Stott et al (2004) and Haley (2004), the increase in Danish Autism rates is due to "greater diagnostic awareness," for prior to 1994 there were "limitations of the [Danish] symptomatic classification of childhood developmental disorders" (Stott et al, 2004). Furthermore, classification adjustments in 1994 resulted in an increase in Autism diagnoses, which resulted in the apparent increase in the prevalence of Danish Autism rates (Stott et al, 2004). While although numerous U.S. studies have discounted the benefits of Denmark's removal of mercury preservatives from vaccines, it is important to note that the current "elevated" Autism rate in Demark, is a lower level than what has been considered the "pre-epidemic" rate of Autism (3-5 per 10,000) in the United States during the 1980s (Haley, 2004).

Although it is difficult to clearly determine whether the removal of Thimerosal from vaccines has been successful so far in lowering Autism rates in the United States, Olmsted's (2005) observations of the Amish offers significant insight. For as a non-vaccinated population, the Amish represent a control group within the United States population. In interviewing the medical director of a large health service practice, which serves an Amish community in Illinois, Olmsted (2005) finds that Autism is nearly irrelevant within the Amish community. In having cared for 30,000 to 35,000 children, the director can only recall two or three cases of Autism since founding his practice in 1973. While it is important to note that Olmsted's (2005) findings are purely observational and not scientific in nature, and also that other factors may be causing the low rate of Autism among the Amish, this connection does suggest a possible link between Thimerosal and Autism.

Much progress has been made to date in removing or reducing Thimerosal in vaccines, however, public concern remains great about the safety of children's vaccines and about the plausibility of a link between increased mercury exposure and Autism. In efforts to ease public concern, more research is needed to examine the dynamics of ethyl-

mercury within the human body, so additional policies and regulations can be developed.

Although Thimerosal has been removed from most vaccines used in Europe and North America, developing countries such as India, Argentina, and Nicaragua continue to use Thimerosal containing vaccines, for conditions require preservatives. In addition, while alternative Thimerosal-free preservatives have been developed, such are more costly and are presently available only in limited number.

While many government and independent studies have found Thimerosal not be a cause of Autism, the reliance limited data on ethyl-mercury and flawed and outdated studies about Thimerosal safety suggest Thimerosal may be a contributing factor of Autism. While more research is needed to understand both ethyl-mercury and Thimerosal, in the meantime efforts should be made to remove Thimerosal from *all* vaccines both within United States and globally.

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Table of Appendices

Summary Comparison of Characteristics of Autism & Mercury Poisoning

	Mercury Poisoning	Autism
Psychiatric Disturbances	Social deficits, shyness, social withdrawal	Social deficits, social withdrawal, shyness
	Depression, mood swings; mask face	Depressive traits, mood swings; flat affect
	Anxiety	Anxiety
	Schizoid tendencies, OCD traits	Schizophrenic & OCD traits; repetitiveness
	Lacks eye contact, hesitant to engage others	Lack of eye contact, avoids conversation
	Irrational fears	Irrational fears
	Irritability, aggression, temper tantrums	Irritability, aggression, temper tantrums
	Impaired face recognition	Impaired face recognition
Speech, Language & Hearing Deficits	Loss of speech, failure to develop speech	Delayed language, failure to develop speech
	Dysarthria; articulation problems	Dysarthria; articulation problems
	Speech comprehension deficits	Speech comprehension deficits
	Verbalizing & word retrieval problems	Echolalia; word use & pragmatic errors
	Sound sensitivity	Sound sensitivity
	Hearing loss; deafness in very high doses	Mild to profound hearing loss
	Poor performance on language IQ tests	Poor performance on verbal IQ tests
Sensory Abnormalities	Abnormal sensation in mouth & extremities	Abnormal sensation in mouth & extremities
	Sound sensitivity	Sound sensitivity
	Abnormal touch sensations; touch aversion	Abnormal touch sensations; touch aversion
	Vestibular abnormalities	Vestibular abnormalities
Motor Disorders	Involuntary jerking movements – arm flapping, ankle jerks, myoclonal jerks, choreiform movements, circling, rocking	Stereotyped movements - arm flapping, jumping, circling, spinning, rocking; myoclonal jerks; choreiform movements
	Deficits in eye-hand coordination; limb apraxia; intention tremors	Poor eye-hand coordination; limb apraxia; problems with intentional movements
	Gait impairment; ataxia – from incoordination & clumsiness to inability to	Abnormal gait and posture, clumsiness and

	incoordination & clumsiness to inability to walk, stand, or sit; loss of motor control	clumsiness and incoordination; difficulties sitting, lying, crawling, and walking
	Difficulty in chewing or swallowing	Difficulty chewing or swallowing
	Unusual postures; toe walking	Unusual postures; toe walking
Cognitive Impairments	Borderline intelligence, mental retardation - some cases reversible	Borderline intelligence, mental retardation - sometimes "recovered"
	Poor concentration, attention, response inhibition	Poor concentration, attention, shifting attention
	Uneven performance on IQ subtests	Uneven performance on IQ subtests
	Verbal IQ higher than performance IQ	Verbal IQ higher than performance IQ
	Poor short term, verbal, & auditory memory	Poor short term, auditory & verbal memory
	Poor visual and perceptual motor skills, impairment in simple reaction time	Poor visual and perceptual motor skills, lower performance on timed tests
	Difficulty carrying out complex commands	Difficulty carrying out multiple commands
	Word-comprehension difficulties	Word-comprehension difficulties
	Deficits in understanding abstract ideas & symbolism; degeneration of higher mental powers	Deficits in abstract thinking & symbolism, understanding other's mental states, sequencing, planning & organizing

Unusual Behaviors	Stereotyped sniffing (rats)	Stereotyped, repetitive behaviors
	ADHD traits	ADHD traits
	Agitation, unprovoked crying, grimacing, staring spells	Agitation, unprovoked crying, grimacing, staring spells
	Sleep difficulties	Sleep difficulties
	Eating disorders, feeding problems	Eating disorders, feeding problems
	Self injurious behavior, e.g. head banging	Self injurious behavior, e.g. head banging
Visual Impairments	Poor eye contact, impaired visual fixation	Poor eye contact, problems in joint attention
	"Visual impairments," blindness, near-sightedness, decreased visual acuity	"Visual impairments"; inaccurate/slow saccades;

	sightedness, decreased visual acuity	inaccurate/slow saccades; decreased rod functioning
	Light sensitivity, photophobia	Over-sensitivity to light
	Blurred or hazy vision	Blurred vision
	Constricted visual fields	Not described
Physical Disturbances	Increase in cerebral palsy; hyper- or hypo-tonia; abnormal reflexes; decreased muscle strength, especially upper body; incontinence; problems chewing, swallowing, salivating	Increase in cerebral palsy; hyper- or hypotonia; decreased muscle strength, especially upper body; incontinence; problems chewing and swallowing
	Rashes, dermatitis/dry skin, itching; burning	Rashes, dermatitis, eczema, itching
	Autonomic disturbance: excessive sweating, poor circulation, elevated heart rate	Autonomic disturbance: unusual sweating, poor circulation, elevated heart rate
Gastro-intestinal Disturbances	Gastroenteritis, diarrhea; abdominal pain, constipation, "colitis"	Diarrhea, constipation, gaseousness, abdominal discomfort, colitis
	Anorexia, weight loss, nausea, poor appetite	Anorexia; feeding problems/vomiting
	Lesions of ileum & colon; increased gut permeability	Leaky gut syndrome
	Inhibits dipeptidyl peptidase IV, which cleaves casomorphin	Inadequate endopeptidase enzymes needed for breakdown of casein & gluten
Abnormal Biochemistry	Binds -SH groups; blocks sulfate transporter in intestines, kidneys	Low sulfate levels
	Has special affinity for purines & pyrimidines	Purine & pyrimidine metabolism errors lead to autistic features
	Reduces availability of glutathione, needed in neurons, cells & liver to detoxify heavy metals	Low levels of glutathione; decreased ability of liver to detoxify heavy metals
	Causes significant reduction in glutathione peroxidase and glutathione reductase	Abnormal glutathione peroxidase activities in erythrocytes
	Disrupts mitochondrial activities, especially in brain	Mitochondrial dysfunction, especially in brain
Immune Dysfunction	Sensitivity due to allergic or autoimmune reactions; sensitive individuals more likely to have allergies, asthma, autoimmune-like symptoms, especially rheumatoid-like ones	More likely to have allergies and asthma; familial presence of autoimmune diseases, especially rheumatoid arthritis; IgA deficiencies
	Can produce an immune response in CNS	On-going immune response in CNS

	Causes brain/MBP autoantibodies	Brain/MBP autoantibodies present
	Causes overproduction of Th2 subset; kills/inhibits lymphocytes, T-cells, and monocytes; decreases NK T-cell activity; induces or suppresses IFNg & IL-2	Skewed immune-cell subset in the Th2 direction; decreased responses to T-cell mitogens; reduced NK T-cell function; increased IFNg & IL-12

CNS Structural Pathology	Selectively targets brain areas unable to detoxify or reduce Hg-induced oxidative stress	Specific areas of brain pathology; many functions spared
	Damage to Purkinje and granular cells	Damage to Purkinje and granular cells
	Accummulates in amygdala and hippocampus	Pathology in amygdala and hippocampus
	Causes abnormal neuronal cytoarchitecture; disrupts neuronal migration & cell division; reduces NCAMs	Neuronal disorganization; increased neuronal cell replication, increased glial cells; depressed expression of NCAMs
	Progressive microcephaly	Progressive microcephaly and macrocephaly
	Brain stem defects in some cases	Brain stem defects in some cases
Abnormalities in Neuro-chemistry	Prevents presynaptic serotonin release & inhibits serotonin transport; causes calcium disruptions	Decreased serotonin synthesis in children; abnormal calcium metabolism
	Alters dopamine systems; peroxidine deficiency in rats resembles mercurialism in humans	Possibly high or low dopamine levels; positive response to peroxidine (lowers dopamine levels)
	Elevates epinephrine & norepinephrine levels by blocking enzyme that degrades epinephrine	Elevated norepinephrine and epinephrine
	Elevates glutamate	Elevated glutamate and aspartate

	Leads to cortical acetylcholine deficiency; increases muscarinic receptor density in hippocampus & cerebellum	Cortical acetylcholine deficiency; reduced muscarinic receptor binding in hippocampus
	Causes demyelinating neuropathy	Demyelination in brain
EEG Abnormalities/	Causes abnormal EEGs, epileptiform activity	Abnormal EEGs, epileptiform activity
	Causes seizures, convulsions	Seizures; epilepsy
Epilepsy	Causes subtle, low amplitude seizure activity	Subtle, low amplitude seizure activities
Population Characteristics	Effects more males than females	Male:female ratio estimated at 4:1
	At low doses, only affects those geneticially susceptible	High heritability - concordance for MZ twins is 90%
	First added to childhood vaccines in 1930s	First "discovered" among children born in 1930s
	Exposure levels steadily increased since 1930s with rate of vaccination, number of vaccines	Prevalence of autism has steadily increased from 1 in 2000 (pre1970) to 1 in 500 (early 1990s), higher in 2000.
	Exposure occurs at 0 - 15 months; clinical silent stage means symptom emergence delayed; symptoms emerge gradually, starting with movement & sensation	Symptoms emerge from 4 months to 2 years old; symptoms emerge gradually, starting with movement & sensation

Source: Autism Research Institute. (2008). Retrieved on April 19 from, http://www.autism.com/triggers/vaccine/mercurylong.htm

Appendix B

Thimerosal Content of Vaccines Routinely Recommended for Children 6 Years of Age and Younger *(updated 7/18/2005*)*

Vaccine	Tradename (Manufacturer)	Thimerosal Status Concentration**(Mercury)	Approval Date for Thimerosal Free or Thimerosal / Preservative Free (Trace Thimerosal)*** Formulation
DTaP	Infanrix (GlaxoSmithKline Biologicals)	Free	Never contained more than a trace of thimerosal, approval date for thimerosal-free formulation 9/29/2000
	Daptacel (Sanofi Pasteur, Ltd)	Free	Never contained Thimerosal
	Tripedia (Sanofi Pasteur, Inc)	Trace(≤0.3 µg Hg/0.5mL dose)	03/07/01
DTaP-HepB-IPV	Pediarix (GlaxoSmithKline Biologicals)	Free	Never contained more than a Trace of Thimerosal, approval date for thimerosal-free formulation 1/29/2007
Pneumococcal conjugate	Prevnar (Wyeth Pharmaceuticals Inc)	Free	Never contained Thimerosal
Inactivated	IPOL	Free	Never contained

Poliovirus	(Sanofi Pasteur, SA)		Thimerosal
Varicella (chicken pox)	Varivax (Merck & Co, Inc)	Free	Never contained Thimerosal
Mumps, measles, and rubella	M-M-R-II (Merck & Co, Inc)	Free	Never contained Thimerosal
Hepatitis B	Recombivax HB (Merck & Co, Inc)	Free	08/27/99
	Engerix B (GlaxoSmithKline Biologicals)	Free	03/28/00, approval date for thimerosal-free formulation 1/30/2007
Haemophilus influenzae type b conjugate (Hib)	ActHIB (Sanofi Pasteur, SA) OmniHIB (GlaxoSmithKline)	Free	Never contained Thimerosal
	PedvaxHIB (Merck & Co, Inc)	Free	08/99
	HibTITER, single dose (Wyeth Pharmaceuticals, Inc.)[1]	Free	Never contained Thimerosal
Hib/Hepatitis B combination	Comvax (Merck & Co, Inc)	Free	Never contained Thimerosal
Influenza	Fluzone (Sanofi Pasteur, Inc)	0.01% (12.5 µg/0.25 mL dose, 25 µg/0.5 mL dose)[2]	
	Fluzone (Sanofi Pasteur, Inc)[3] (no thimerosal)	Free	12/23/2004

	Fluvirin (Novartis Vaccines and Diagnostics Ltd)	0.01% (25 µg/0.5 mL dose)	
	Fluvirin (Novartis Vaccines and Diagnostics Ltd) (Preservative Free)	Trace (<1ug Hg/0.5mL dose)	09/28/01
Influenza, live	FluMist (MedImmune Vaccines, Inc)	Free	Never contained Thimerosal

** Thimerosal is approximately 50% mercury (Hg) by weight. A 0.01% solution (1 part per 10,000) of thimerosal contains 50 µg of Hg per 1 mL dose or 25 µg of Hg per 0.5 mL dose.
*** The term "trace" has been taken in this context to mean 1 microgram of mercury per dose or less.
[1] HibTiITER was also manufactured in thimerosal-preservative containing multidose vials but these were no longer available after 2002.
[2] Children 6 months old to less than 3 years of age receive a half-dose of vaccine, i.e., 0.25 mL; children 3 years of age and older receive 0.5 mL.
[3] A trace thimerosal containing formulation of Fluzone was approved on 9/14/02 and has been replaced with the formulation without thimerosal.

Source: Food and Drug Administration, FDA. (2008). Thimerosal in vaccines. Retrieved March 8, 2008 from http://www.fda.gov/CBER/vaccine/thimerosal.htm.

Appendix C

Preservatives Used in U.S. Licensed Vaccines

Preservative	Vaccine Examples (Tradename; Manufacturer)
Thimerosal	DT Td (several) TT (several) Influenza (several)
2-phenoxyethanol and formaldehyde	IPV (IPOL; Sanofi Pasteur, SA) DTaP (Daptacel; Sanofi Pasteur, Ltd)
Phenol	Typhoid Vi Polysaccharide (Typhim Vi; Sanofi Pasteur, SA) Pneumococcal Polysaccharide (Pneumovax 23; Merck & Co, Inc)
Benzethonium chloride (Phemerol)	Anthrax (Biothrax; BioPort Corporation)
2-phenoxyethanol	DTaP (Infanrix; GlaxoSmithKline Biologicals) Hepatitis A/Hepatitis B (Twinrix; GlaxoSmithKline Biologicals)

Source: Food and Drug Administration, FDA. (2008). Thimerosal in vaccines. Retrieved March 8, 2008 from http://www.fda.gov/CBER/vaccine/thimerosal.htm.

Appendix D

Thimerosal Content in Currently Manufactured U.S. Licensed Vaccines

(updated 3/14/2008)

Vaccine	Trade Name	Manufacturer	Thimerosal Concentration[1]	Mercury
Anthrax	Anthrax vaccine	BioPort Corporation	0	0
DTaP	Tripedia[2]	Sanofi Pasteur, Inc	≤ 0.00012%	≤ 0.3 µg/0.5 mL dose
	Infanrix	GlaxoSmithKline Biologicals	0	0
	Daptacel	Sanofi Pasteur, Ltd	0	0
DTaP-HepB-IPV	Pediarix	GlaxoSmithKline Biologicals	0	0
DT	No Trade Name	Sanofi Pasteur, Inc	< 0.00012% (single dose)	< 0.3 µg/0.5mL dose
		Sanofi Pasteur, Ltd[3]	0.01%	25 µg/0.5 mL dose
Td	No Trade Name	Mass Public Health	0.0033%	8.3 µg/0.5 mL dose
	Decavac	Sanofi Pasteur, Inc	≤ 0.00012%	≤ 0.3 µg mercury/0.5 ml dose
	No Trade Name	Sanofi Pasteur, Ltd	0	0
Tdap	Adacel	Sanofi Pasteur, Ltd	0	0
	Boostrix	GlaxoSmithKline Biologicals	0	0
TT	No Trade Name	Sanofi Pasteur, Inc	0.01%	25 µg/0.5 mL dose
Hib	ActHIB/OmniHIB[4]	Sanofi Pasteur,	0	0

		SA		
	HibTITER	Wyeth Pharmaceuticals, Inc.	0	0
	PedvaxHIB liquid	Merck & Co, Inc	0	0
Hib/HepB	COMVAX[5]	Merck & Co, Inc	0	0
Hepatitis B	Engerix-B Pediatric/adolescent Adult	GlaxoSmithKline Biologicals	< 0.0002% < 0.0002%	< 0.5 µg/0.5 mL dose <1µg/1 ml dose
	Recombivax HB Pediatric/adolescent Adult (adolescent) Dialysis	Merck & Co, Inc	 0 0 0	 0 0 0
Hepatitis A	Havrix	GlaxoSmithKline Biologicals	0	0
	Vaqta	Merck & Co, Inc	0	0
HepA/HepB	Twinrix	GlaxoSmithKline Biologicals	< 0.0002%	< 1 µg/1mL dose
IPV	IPOL	Sanofi Pasteur, SA	0	0
	Poliovax	Sanofi Pasteur, Ltd	0	0
Influenza	Afluria	CSL Limited	0 (single dose) 0.01% (multidose)	0/0.5 mL (single dose) 24.5 µg/0.5 mL (multidose)
	Fluzone[6]	Sanofi Pasteur, Inc	0.01%	25 µg/0.5 mL dose
	Fluvirin	Novartis Vaccines and Diagnostics Ltd	0.01%	25 µg/0.5 ml dose
	Fluzone (no	Sanofi Pasteur,	0	0

	thimerosal)	Inc		
	Fluvirin (Preservative Free)	Novartis Vaccines and Diagnostics Ltd	< 0.0004%	< 1 µg/0.5 mL dose
	Fluarix	GlaxoSmithKline Biologicals	< 0.0004%	< 1 µg/0.5 ml dose
	FluLaval	ID Biomedical Corporation of Quebec	0.01%	25 µg/0.5 ml dose
Influenza, live	FluMist	MedImmune Vaccines, Inc	0	0
Japanese Encephalitis[7]	JE-VAX	Research Foundation for Microbial Diseases of Osaka University	0.007%	35 µg/1.0mL dose 17.5 µg/0.5 mL dose
MMR	MMR-II	Merck & Co, Inc	0	0
Meningococcal	Menomune A, C, AC and A/C/Y/W-135	Sanofi Pasteur, Inc	0.01% (multidose) 0 (single dose)	25 µg/0.5 dose 0
	Menactra A, C, Y and W-135	Sanofi Pasteur, Inc	0	0
Pneumococcal	Prevnar (Pneumo Conjugate)	Wyeth Pharmaceuticals Inc	0	0
	Pneumovax 23	Merck & Co, Inc	0	0
Rabies	IMOVAX	Sanofi Pasteur, SA	0	0
	Rabavert	Novartis Vaccines and Diagnostics	0	0
Smallpox (Vaccinia), Live	ACAM2000	Acambis, Inc.	0	0
Typhoid Fever	Typhim Vi	Sanofi Pasteur, SA	0	0
	Vivotif	Berna Biotech,	0	0

		Ltd		
Varicella	Varivax	Merck & Co, Inc	0	0
Yellow Fever	Y-F-Vax	Sanofi Pasteur, Inc	0	0

Table Footnotes

1. Thimerosal is approximately 50% mercury (Hg) by weight. A 0.01% solution (1 part per 10,000) of thimerosal contains 50 µg of Hg per 1 ml dose or 25 µg of Hg per 0.5 ml dose.
2. Sanofi Pasteur's Tripedia may be used to reconstitute ActHib to form TriHIBit. TriHIBit is indicated for use in children 15 to 18 months of age.
3. This vaccine is not marketed in the US.
4. OmniHIB is manufactured by Sanofi Pasteur but distributed by GlaxoSmithKline.
5. COMVAX is not licensed for use under 6 weeks of age because of decreased response to the Hib component.
6. Children under 3 years of age receive a half-dose of vaccine, i.e., 0.25 mL (12.5 µg mercury/dose.)
7. JE-VAX is distributed by Aventis Pasteur. Children 1 to 3 years of age receive a half-dose of vaccine, i.e., 0.5 mL (17.5 µg mercury/dose).

Source: Food and Drug Administration, FDA. (2008). Thimerosal in vaccines. Retrieved March 8, 2008 from http://www.fda.gov/CBER/vaccine/thimerosal.htm.

Appendix E

Thimerosal Content in Some US Licensed Vaccines

Vaccine	Brand Name (click on the brand name for package insert)		Manufacturer	Thimerosal Concentration[1]	Mercury mcg/0.5 ml
nthrax	BioThrax		BioPort Corporation	0	0
TaP	Tripedia		sanofi pasteur	*	*
	Infanrix		GlaxoSmithKline	0	0
	DAPTACEL		sanofi pasteur	0	0
TaP-HepB-IPV	Pediarix		GlaxoSmithKline	0	0
TaP-Hib	TriHIBit		sanofi pasteur	*	*
TwP	All Products			.01%	25
T	Diphtheria & Tetanus Toxoids Adsorbed USP	multi-dose	sanofi pasteur	.01%	25
		single dose		*	*
d	DECAVAC		sanofi pasteur	*	*
	Tetanus and Diphtheria Toxoids Adsorbed		sanofi pasteur	*	*
dap	ADACEL		sanofi pasteur	0	0
	Boostrix		GlaxoSmithKline	0	0
etanus Toxoid	Tetanus Toxoid Adsorbed USP		sanofi pasteur	.01%	25
	Tetanus Toxoid Adsorbed Adult Use			.01%	25
	Booster			.01%	25
Hib	ActHIB		sanofi pasteur	0	0
	HibTITER		Wyeth-Ayerst	0	0
	PedvaxHIB liquid(2)		Merck	0	0
Hib/HepB	Comvax (3)		Merck	0	0
Hepatitis A	Havrix		GlaxoSmithKline	0	0
	Vaqta adult/pediatric		Merck	0	0
Hepatitis B	Engerix-B preservative free		GlaxoSmithKline	0	0
	Recombivax HB preservative free		Merck	0	0
Hep A-B	Twinrix		GlaxoSmithKline	*	*
HPV	Gardasil		Merck	0	0
Influenza 2007/8 Formula	Afluria	multi-dose	CSL Limited	.01%	24.5
		single dose		0	0
	Fluarix		GlaxoSmithKline	*	*
	FluLaval		GlaxoSmithKline	.01%	25
	FluMist		MedImmune	0	0
	Fluvirin		Novartis	.01%	24.5
	Fluzone	5 mL vial	sanofi pasteur	.01%	25
	Fluzone No Preservative			0	0

V	IPOL		sanofi pasteur	0	0
eningococcal	Menactra		sanofi pasteur	0	0
	MENOMUNE-A/C/Y/W-135	multi-dose	sanofi pasteur	.01%	25
		single dose		*	*
MR	M-M-R II		Merck	0	0
MR-Varicella	ProQuad		Merck	0	0
olio	IPOL		sanofi pasteur	0	0
neumococcal	Prevnar		Wyeth-Ayerst	0	0
	Pneumovax 23		Merck	0	0
abies	RabAvert		Chiron	0	0
	IMOVAX		sanofi pasteur	0	0
otavirus	RotaTeq		Merck	0	0
yphoid Fever	Typhim Vi		sanofi pasteur	0	0
	Vivotif		Berna Biotch	0	0
aricella Zoster	Varivax		Merck	0	0
	Zostavax		Merck	0	0
ellow Fever	YF-VAX		sanofi pasteur	0	0

. *A concentration of 1:10,000 is equivalent to a 0.01% concentration. Thimerosal is approximately 50% Hg by weight. A 1:10,000 concentration ontains 25 micrograms of Hg per 0.5 mL.*

. *A previously marketed lyophilized preparation contained 0.005% thimerosal.*

. *COMVAX is not approved for use under 6 weeks of age because of decreased response to the Hib component.*

This product should be considered equivalent to thimerosal-free products. This vaccine may contain trace amounts (<0.3 mcg) of mercury left fter post-production thimerosal removal; these amounts have no biological effect. JAMA 1999;282(18) and JAMA 2000;283(16).

Source: Institute for Vaccine Safety.(2008). Thimerosal content in some US licensed vaccines. Retrieved March 8, 2008 from http://www.vaccinesafety.edu/thi-table.htm